"Synthesis and Analysis of novel triazolo thiadiazole derivatives as a biological interest" Review

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***Abstract*—** Heterocyclic compounds are highly attracted to medical chemicals due to their unique chemical properties and wide range of biological activity. Triazolo-thiadiazole and related fused heterocyclic compounds are of interest as potential bioactive molecules.Triazolo-thiadiazole extracts are highly sensitive to organic chemicals due to their biological and chemotherapeutic value.Research in the field of anti-mycobacterium, anti-inflammatory and anti-microbial therapy is continuous ongoing and demanding study. Hence, the search for newer effective anti-mycobacterium, anti-inflammatory and antimicrobial agent is imperative.

The need of new anti-microbial, anti-mycobacterial agents is justified because more microorganisms are being resistant to the present drugs available in the market. Worldwide researchers are trying to synthesize new drugs with better pharmacokinetic and dynamic properties with less adverse effects.The literature survey suggests that the fuse ring of Triazolo-thiadiazole derivatives have proved to be good bioactive molecules. They have shown diverse biological activities like anti-bacterial, anti-fungal, anti-inflammatory, anti-tubercular, anticancer, anticonvulsant, antioxidant, analgesic, etc.Therefore, in view of above facts it was thought of interest to synthesize some Triazolo-thiadiazole derivatives.

Triazolo-thiadiazole has played a crucial role in the history of chemistry. Owing to their versatile chemotherapeutics importance, significant research efforts have been made on these nuclei. The literature review suggested that Triazolo-thiadiazole possesses wide and potent activity as an antibacterial, anti-inflammatory, anti-diabetics, and anti-tubercular agent.Hence, there is a need to develop an efficient and yield-oriented process for the preparation of such derivatives.

***Keywords*—** Triazolo-thiadiazole, antibacterial, anti-diabetic, Antitubercular, and Anti-inflammatory**.**

I. INTRODUCTION

Medical chemical advice is given to the discovery and development of new agents in the treatment of diseases. Most of this work is focused on chemical or synthetic materials. Heterocyclic ingredients are popular in therapeutic chemicals due to their unique chemical properties and wide range of functions. The discovery of the discovery has been an important part and is aimed at reversing drug action, especially to reduce side effects and cause drug action. Organic molecules have direct growth activities of drugs that apparently have great potential.The development of organic compounds has grown beyond traditional synthetic methods despite significant research progress on heterocyclic ring systems. Efforts are going to identify novel heterocyclic compounds with potent bioactivities.Today more than 60% of the drugs used in the use are derived from other synthetic products and day by day the number of synthetic ingredients increases.

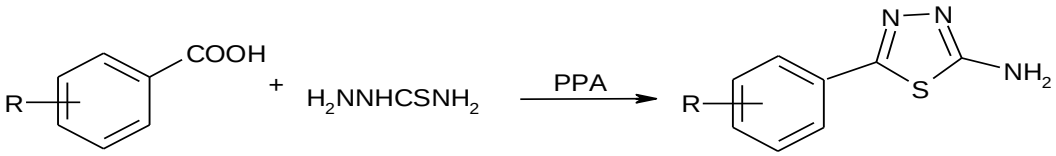
Much effort has been put into making and developing novel drugs from artificial origin. Therefore, there is a growing interest in pharmacological capacity.Triazolo-thiadiazole and related fused heterocyclic compounds are of interest as potential bioactive molecules. Triazolo-thiadiazole extracts are highly sensitive to organic chemicals due to their biological and chemotherapeutic value. In many cases, heterocyclic ring formation has led to a wide range of biological functions.Some of the activities possessed by heterofused Triazolo-thiadiazole include antibacterial, anti-inflammatory, anti-diabetics and anti-tubercular etc.

Chemistry itself affects mainly the organic, analytical, and biochemical factor in this process, but the chemist must successfully interact with those in other abilities.The process of establishing new pharmaceuticals is exceeding complex and involves the talents of the people from a variety of disciplines including chemistry, biochemistry, molecular biology, physiology, pharmacology, pharmaceutics, and medicine. Thus, the medical chemist replaces the most common visible chemistry and biology.

Thousands of new organic compounds are synthesized annually throughout the world and hundreds of them are entered into pharmacological screens to determine whether they have useful biological activity. Only a few of them are coming to the clinical trials. This process of random screening has been considered insufficient, but it has resulted in the identification of new lead compounds whose structures have been optimized to produce clinical agents. In some cases, lead is grown by closely observing the pharmacological behavior of an existing drug. Much effort has been put into making and developing novel drugs from artificial origin. Therefore, there is a growing interest in pharmacological capacity.

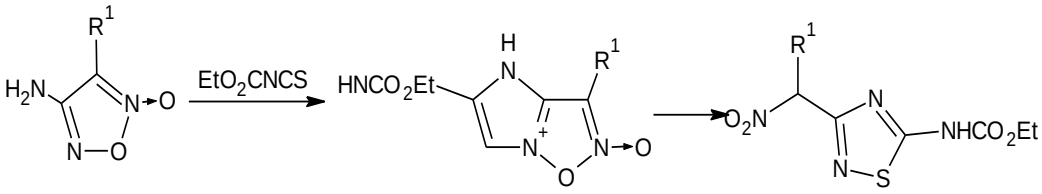
2 MAIN TEXT

Turner et al. have prepared 2-amino-5-aryl 1,3,4-thiadiazoles directly by heating a mixture of the acid and thiosemicarbazide with PPA, e.g.



Where R = 2-SCH_3, 2-$SOCH_3$, 2,6$(OCH_3)_2$ etc.

Vivona et al. have synthesized 5-amino-3-(a-nitroalkyl)-1,2,4-thiadiazoles have been obtained by thermal rearrangements in 3-substituted 4-(3-ethoxycarbonyl thioureido)-1,2,5-oxadiazole 2-oxides.The reaction was performed by re-mixing the mixture of aminofuroxans with ethoxy carbonyl isothiocyanate into organic solvent.

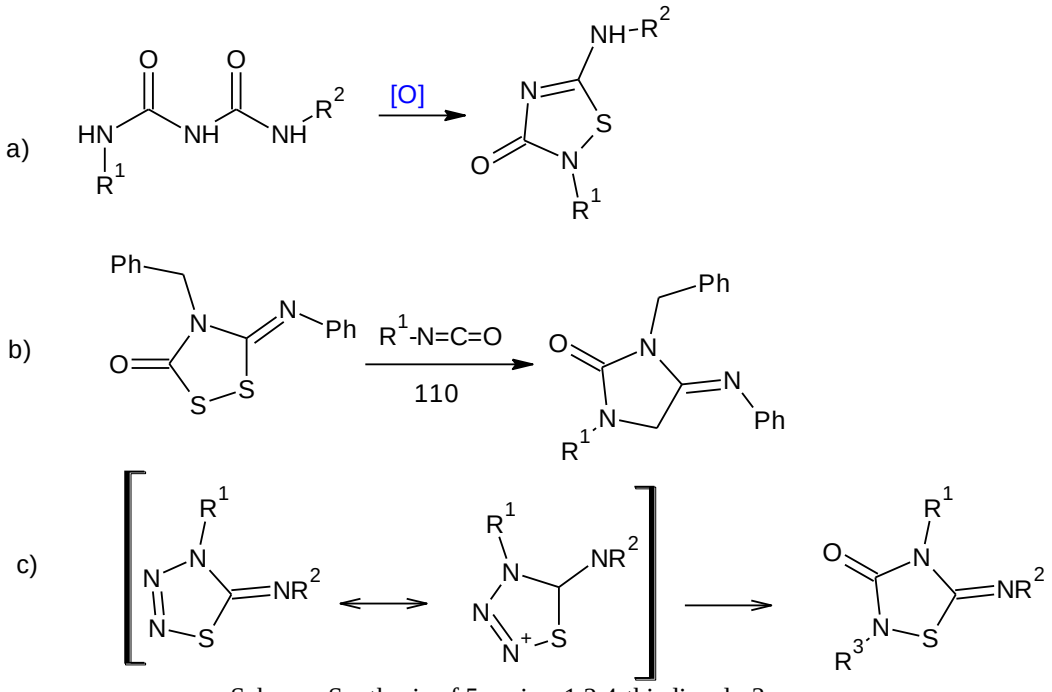


Scheme - Thermal regeneration of 3 substitutes 4 (3-ethoxycarbonylthioureido) - 1,2,5-oxadiazole 2-oxides.

Paiet al. have synthesized 5-amino-1,2,4-thiadiazole- 3-ones was achieved by ring closure of thiobiurets in the presence of different oxidizing agents. In this way, 5-amino-1,2,4-thiadiazole- 3-ones were obtained via N–S bond formation with hydrogen peroxide in an alkaline solution. Other oxidizing agents such as molecular bromine and N-bromosuccinimidewere used for cyclization (Scheme a).

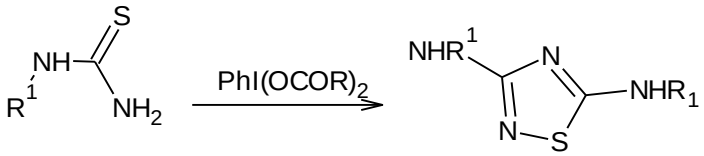
Choet al.have synthesized 1,2,4-thiadiazole ring has been prepared from other heterocycles by a cycloaddition–elimination sequence. The reaction of 5-benzylimino-1,2,4-dithiazolidin-3-one with isocyanates .(Scheme b).

Singh et al. have synthesized 5-imino-1,2,4-thiadiazole- 3-ones is by using 5-imino-1,2,3,4-thiatriazolinesas masked 1,3-dipoles with isocyanates via cycloaddition– elimination reactions (Scheme c).



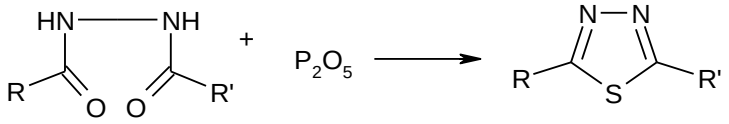
Scheme .Synthesis of 5-amino-1,2,4-thiadiazole-3-one.

Mamaeva et al.have modified the oxidation of thioureas binary compounds used as a standard method for the preparation of different 1,2,4-thiadiazole alternatives by intramolecular heterocyclization procedures. Recently, 3.5-diamino-1,2,4- thiadiazoles have been identified using [bis (acyloxy) iodo] arenes as a more specific oxidant reagent than traditional (Scheme).



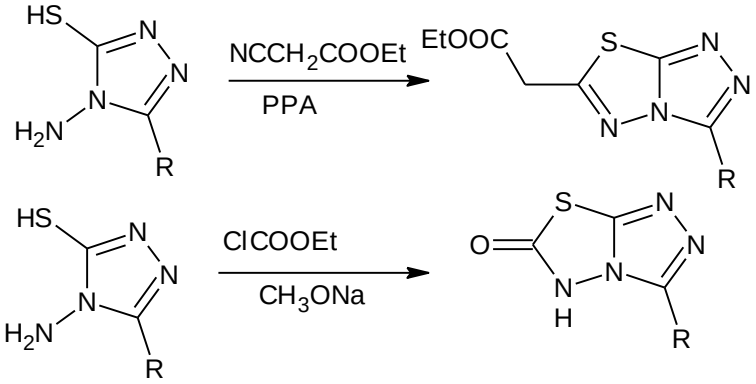
Scheme .Synthesis of 3,5-diamino-1,2,4-thiadiazoles.

Stolle et al. prepared a total of 2,5-dialkyl-1,3,4-thiadiazoles from 1,2-diacylhydrazines and P_2S_5.e.g.

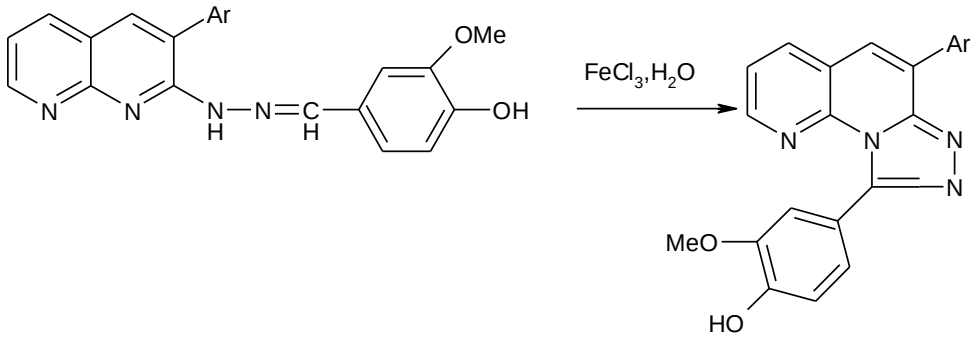


Instead of using P_2S_5, 1,2-diacylhydrazine thiacylation is affected by carboxymethyldithioate, where heating provides 2.5-disubstituted thiadiazoles.

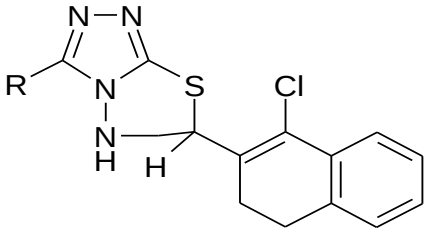
Shehryet al.have synthesized 3-((2,4-dichlorophenoxy)methyl)-1,2,4-triazolo(thiadiazoles and thiadiazines) as anti-inflammatory and molluscicidalagents.



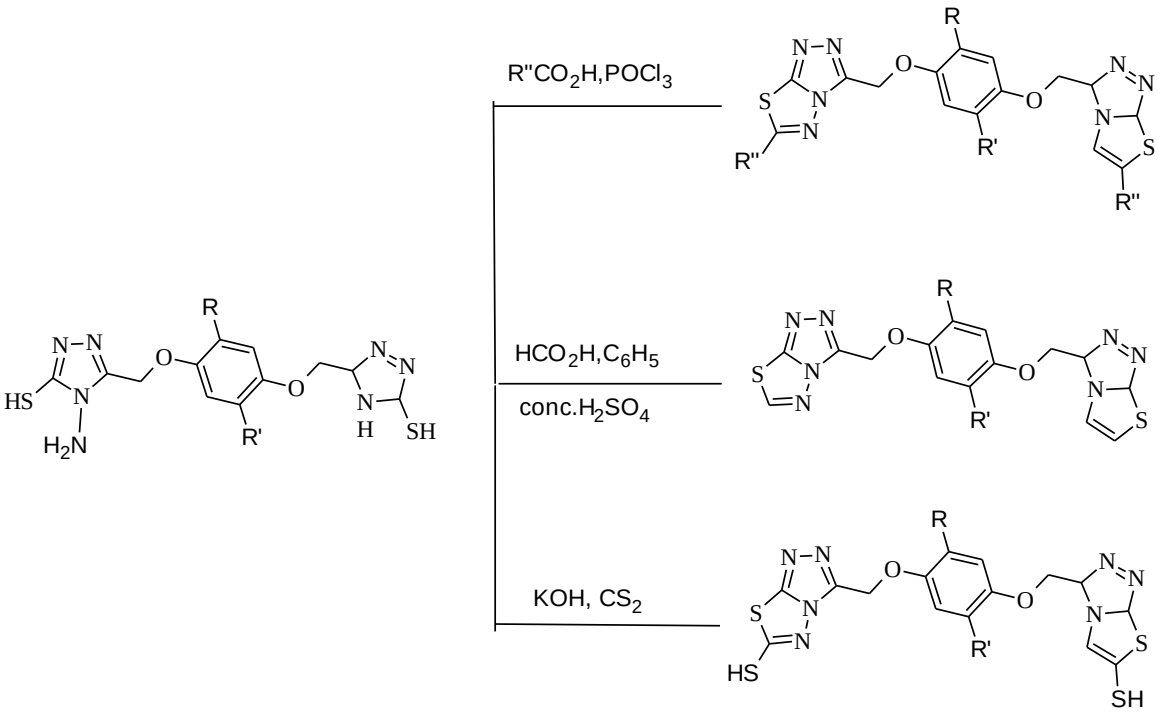
Mogilaiahet al.have prepared solid-phase synthesis of Triazole using $FeCl_3$ using Oxidative cyclization[], An efficient and mild method for the synthesis of 1,2,4-Triazole by Oxidative circulation in a solid state by grinding at room temperature has been described.



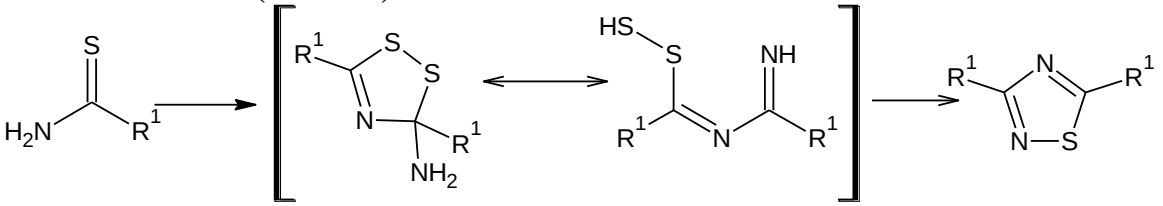
Padhy et al. have synthesized microwave-assisted synthesis of 1, 2, 4-Triazole derivatives, The 1,2,4-Triazoles can be synthesized using a catalytic amount of p-TsOH under Microwave irradiation rate enhancement and improvement in yields



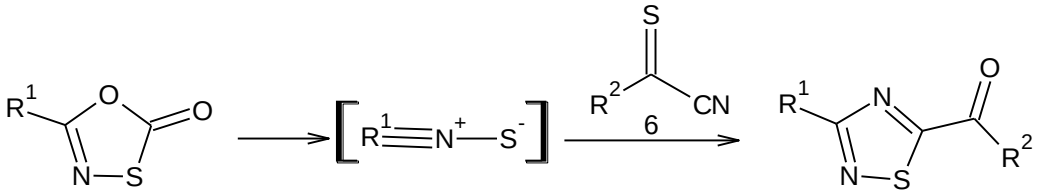
Hollaet al. have synthesized bis- amino-mercapto triazoles and bis-triazolothiadiazoles as possible anticancer agents.



McKieet al. have synthesized 3,5-diaryl/dialkyl- 1,2,4-thiadiazole usually includes an oxidation step of compounds containing the thioamide group. A variety of oxidizing agents as halogens, hydrogen peroxide or thionyl chloride yield 3,5-disubstituted 1,2,4-thiadiazole after cyclization reactions in moderate yields. Recently, it has been reported on the condensation reaction of thioamides in the presence of oxidative DMSO–HCl mixtures. This route has proved to be suitable to obtain symmetrically substituted derivatives (Scheme 1a).

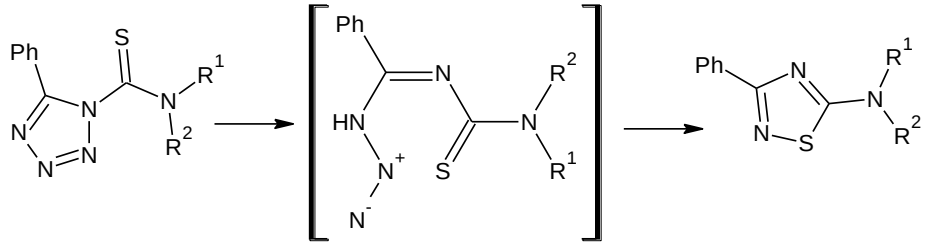


Pavlik et al.have prepared the most widely used routes to nitrile sulfides are based on the thermal decarboxylation at 130–160 ^{0}C of 1,3,4- oxathiazol-2-ones , which are stable at room temperature and readily accessible (Scheme 1b).



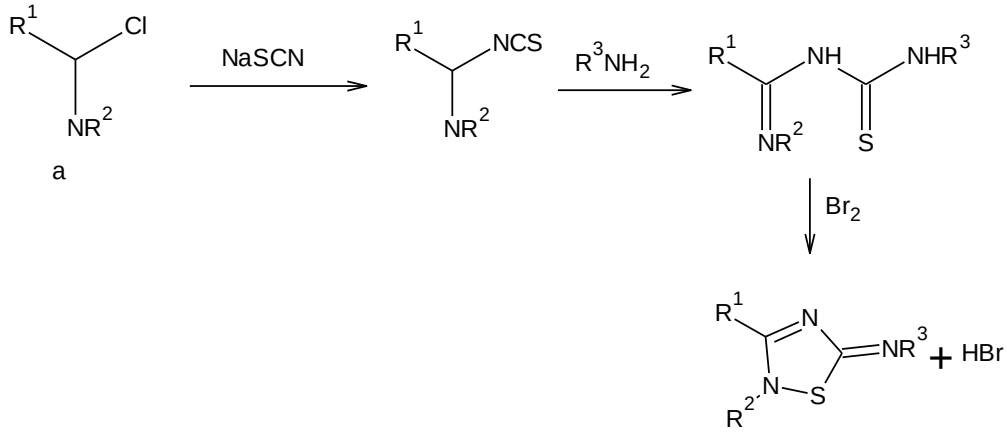
Scheme :Synthesis of 3,5-diaryl/dialkyl-1,2,4-thiadiazole

Molotov et al.have composed of 3-Alkyl-5-amino-1,2,4-thiadiazole produced by thermolysis of various five-marking rings. Using the method of oxathiadiazole thermolysis, the reaction of nitrile sulfide produced by tosyl cyanide produced a medium-sized key containing labile tosyl instead of five thiadiazole positions. The dissolution of the tosyl group with ammonia was given 5- amino-3-instead amediazoles. These heterocycles are also produced by thermolysis of 1-thiocarbamoyl-5-phenyl-tetrazoles (Scheme).



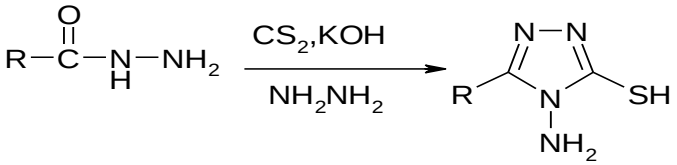
Scheme: Synthesis of 3-substituted-5-amino-1,2,4-thiadiazole by thermolysis.

Pattan et al.have synthesized besides thermolysis and rearrangements, 1,2,4-thiadiazoles have been obtained by oxidative formation from imidoylthioureas (Scheme 6).To prepare the compounds, benzamides were used as starting materials that were converted into benzimidoyl chlorides . Substitution of the chlorine atom in the compound a by anSCNmoiety to form intermediate, followed by the addition of an amine, afforded thioureas and in the last step, oxidation with bromine yield 2,3,5-substititute [1,2,4] -thiadiazoles referred to as hydrobromide salts.

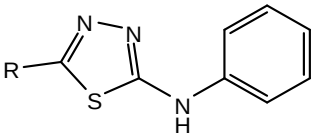


Scheme: Synthesis of 1,2,4-thiadiazole via imidoyl chlorides.

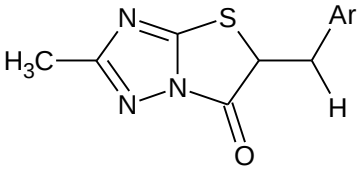
Sayed REet al. have synthesized1, 2, 4-Triazole derivatives can also be prepared using Hydrazides, Carbon disulfide in presence of Base. Synthesis, antibacterial, and topical activity of 1,2,4-triazole derivatives.



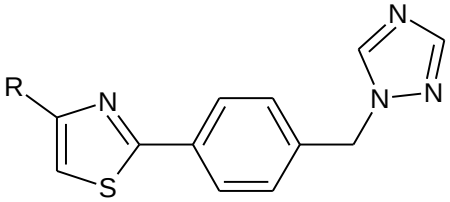
Nida N. Farshoriet al has synthesized oxadiazoles and thiadiazoles have been screened for antibacterial and antifungal activities. The investigation of antimicrobial screening revealed that compounds show good antibacterial and antifungal activities.



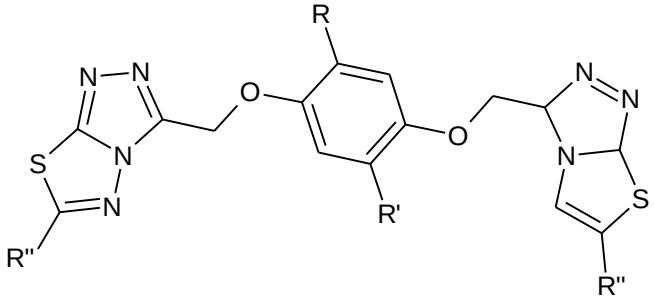
Birsen Tozkoparana et al. use 6-Benzylidenethiazolo [3, 2-b] -1, 2, 4-triazole-5 (6H) -deleted instead of ibuprofen and tested for anti-inflammatory activity.



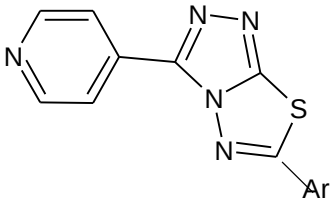
John Jaya et al.have contains thiazole-based 2, 4-disubstitized thiazole containing 1, 2, 4-triazoles experimental antimicrobial studies.



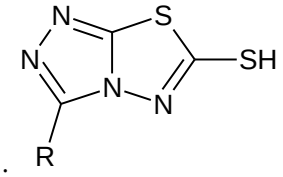
Shivaram Holla et al. has synthesized bis- amino-mercapto triazoles and bis-triazolothiadiazoles as possible anticancer agents.



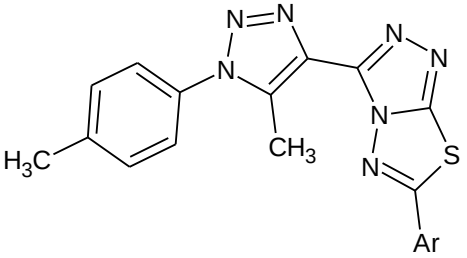
Udupi R H et al. It came with 1,2,4-triazoles from Isoniazid, and had moderate anti-inflammatory activity and anti-inflammatory agents.



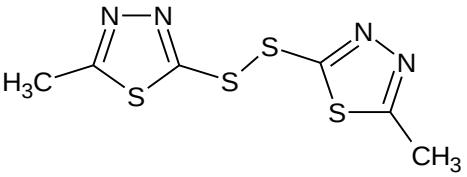
Bhalekar SM. et al have synthesised 1,2,4-triazolo[1,3,4-thiadiazole] derivative.



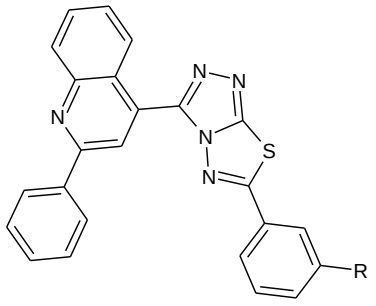
Heng-Shan Dong et al. combine 3- [5-methyl-1- (4-methyl phenyl) -1, 2, 3-triazol-4-yl] -6-instead of s-triazolo [3,4-b] -1,3 , 4-thiadiazoles and their structures established by basic analysis and Spectral data.



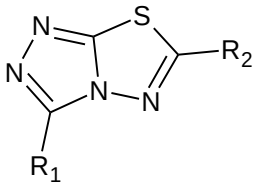
Frank Hipler et al have synthesized Bis(2-methyl-1,3,4- thiadiazolyl)-5,50-disulfide 2, the disulfide, as well as 2-(tert-butyldithio)-5-methyl-1,3,4-thiadiazole 3 and 2,5-bis(tertbutyldithio)- 1,3,4-thiadiazole and characterised by vibrational spectroscopy and X-ray diffraction.



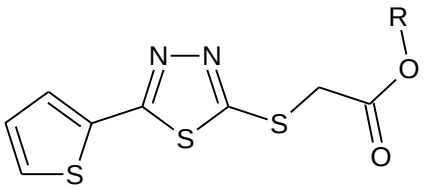
Peng-FeiXu et al. use 2-arylamino-5-cinchophenyl-1,3,4-oxadiazoline (7) and 3-thio-4-amino-5-cinchophenyl- 1,2,4-triazole using cinchophen as primary ingredients. Other independent compounds were tested for antibacterial activity.



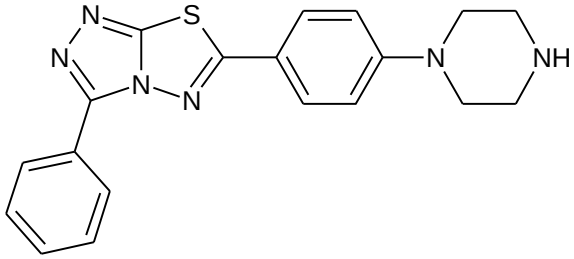
S. Nanjunda Swamy et al developed a double series of 4,6-disubstititan 1,2,4-triazolo-1,3,4-thiadiazole derivatives. The compilation of this article was tested for its effectiveness as a common in vitro antimicrobials. It has shown great efficacy in all tested types, compared to standard drugs.



Alireza Foroumadi et al have synthesized alkyl a-[5-(5-nitro-2-thienyl)-1,3,4-thiadiazole-2-ylthio]acetic acid esters. Also tested for in vitro antituberculosis against Mycobacterium H37Rv using radiometric system BACTEC 460 and BACTEC 12B intermediate



Guo Qiang et al. have synthesized Water-soluble S-Triazolo [3,4 b][1,3,4]thiadiazoles Containing PiperazineGroup.The in vitro biological results showed that the piperazine group conjugated with the above-fused heterocycles played an important role in antibacterial activity.



3 CONCLUSION:

Triazolo-thiadiazole has played a crucial role in the history of chemistry. Owing to their versatile chemotherapeutics importance, significant research efforts have been made on these nuclei. The literature review suggested that Triazolo-thiadiazole possesses wide and potent activity as an antibacterial, anti-inflammatory, anti-diabetics, and anti-tubercular agent.Hence, there is a need to develop an efficient and yield-oriented process for the preparation of such derivatives

4ACKNOWLEDGEMENTS

I thank my esteemed guide Dr.A. K. Sen for his expert guidance during this investigation. His admiration and encouragement always inspired me to pursue the investigation with great interest. My special thanks to the Pravara Rural College of Pharmacy, Pravarnagar for providing the infrastructure and facilities for this research work. I am also grateful to my loving parents and all family members who have been the driving force behind progress and success in every step of my life.

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